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Computerized Misinterpretation of QT Interval in 12-Lead Electrocardiogram and Its Clinical Consequences:ACase of Recurrent Syncope

KanaeHasegawa[1],YoshitomoFukuoka[1],SeikoOhno[2],HiroyasuUzui[1],MinoruHorie[3]andHiroshi Tada[1*]

[1]DepartmentofCardiovascularMedicine,Japan

[2]Department of Bioscience and Genetics, Japan

[3]DepartmentofCardiovascularMedicine,Japan

***Correspondingauthor:**

Tada,
Department of Cardiovascular Medicine Faculty of Medical Sciences,
Eiheiji-cho,Fukui910-1193,Japan,
Tel:+81-776-61-8800,Fax:+81-776-61-8801,
E-mail:htada@u-fukui.ac.jp

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Keywords:

Automateddiagnosis;QTinterval;Syncope;Long QTsyndrome

1. Abstract

The diagnosis of long QT syndrome may be delayed due to absenceofelectrocardiogram(ECG)examinationand/orQTinterval misdiagnosis. We present the case of a patient who took 8 years beforebeingdiagnosedwithlongQTsyndrome.Despitethepresenceofmarked QTprolongationandbimodalTwaves,automated ECGrecordingmisdiagnosedthepatienttobenormal.Thepatient hadrecurrentsyncope;however,repeatECGexaminationwasnot performed because her initial ECG was considered normal. It is crucial in cases of syncope that multiple ECG examinations and physician assessment of findings are performed, without relying exclusively on an automated ECG diagnosis.

2. Abbreviations:ECG:Electrocardiogram**;**QTc:CorrectedQT Interval**;** TdP: Torsades De Pointes

3. Introduction

Patientswithcardiacsyncopehaveincreasedriskofdeath[1],and the occurrence of “syncope” is an important indicator of arrhyth- mic risk [1-3]. Patents with unexplained syncope may have hiddenlongQT syndrome（LQTS） [2].Althoughelectrocardiogram (ECG) isimportant for the diagnosisof LQTS, the diagnosis may be delayed due to absence of ECG examination and/or difficulties of QT interval evaluation [2]. Automated ECG diagnosis has the benefit to reduce the effort of physician for ECG evaluation [4]. However, the automated ECG diagnosis are not always correct,inparticular,QTinterval[5].Wepresentthecaseofapatient

for whom LQTS diagnosis took8 years. Despite the presence of marked QT prolongationand bimodal T waves, automated ECG diagnosis misdiagnosed the patient to be normal at the first synco- pe. The patient had recurrent syncope; however, repeat ECG ex- amination was not performed.

4. CaseReport

A27-year-old female visited our emergency room in the middle of the night because she experienced syncope several times through- out the preceding 2 days upon waking up and when attempting walking at night. At the time of the visit, her consciousness lev- el was clear and plasma potassium concentration was 4.0 mEq/L (normal range: 3.6–4.8 mEq/L). Her 12-lead electrocardiogram(ECG)revealed sinusrhythm(65 beats/min) and QT prolongation with low amplitude T waves (QT/QTc [intervals], 600/640 ms) (Figure 1A). Echocardiography, chest X-ray, and brain magnetic resonance imaging (MRI) findings were normal. She was admitted for follow-up due to the presence of marked QT prolongation on12-leadECG.Fivehoursaftertheadmission,torsadesdepointes (TdP) spontaneously occurred with typical initiating “short- long-short” sequences (Figure 1B) when she felt faintness. Therefore, the patient was clinically diagnosed with long QT syndrome. She had no abnormal ECG findings in past school physical examina- tion. She had no family history of syncope, sudden death, or long QT syndrome (Figure 2A). ECGs of her mother and son showed no QT prolongation (Figure 2A).At the age of 19, the patient expe-

riencednightmaresduringsleep, which werefollowedbyconvulsionsandgroaning.Shefaintedtwiceafterwakinginthemorning. The patient visited a neurology clinic and underwent brain MRI, but the underlying cause remained unknown. At the age of 21,sheexperienceddizziness while walkingortryingto get upinthe morning. She experienced syncope and visited a hospital, where automated ECG diagnosis was within the normal range (Figures 3A, 3B). Brain computed tomography and electroencephalogram revealed no obvious abnormality. Therefore, the physician found no apparent cause for her syncope and she returned her home.The patient continued to have episodes of syncope several timesa year until she the age of 27. Throughout this period, she visited several hospitals and clinics. However, episodes of syncope due to long QT syndrome was not suspected, and the patient did not undergo another ECG examination nor was referred to a cardi- ologist. After admission to our hospital, the ECG recorded at the age of 21 was retrieved and re-evaluated. Her ECG revealed QT prolongationwithnotchedTwaves(Figure3A),afindingthatwas clearlyabnormal(QT/QTc,580/608ms).Geneticanalysisforlong QT syndromeincludingKCNQ1,KCNH2,SCN5A,KCNE1,and KCNE2 was performed after obtaining written informed consent fromthepatient.Anovelframeshiftvariantthatresultedfromduplication (c. 526dupC, p.R176fsX331) in KCNH2 was identified (Figure 2B). Her mother and son, who did not have QT prolongation, did not carry the variant (Figure 2A). The patient was diagnosed with type 2 long QT syndrome. Carvedilol was initiated from 5.0 mg per day, and the dose was gradually increased. One monthlater,herQTintervalhadshortened(QT/QTc,480/488ms), and notched T waves had disappeared (Figure 4A). Two months later,whentaking7.5mgcarvedilolperday,herQTintervalshortenedfurther(QT/QTc,460/460ms)(Figure4B).Aftersixmonths ofreceiving10mgcarvedilolperday,herQTintervalcompletely normalized (QT/QTc,450/442), andT-wave shape was no longer abnormal(Figure4C).Thepatientrecoveredwell,andnosyncope recurrence was observed throughout a 3-year follow-up period.

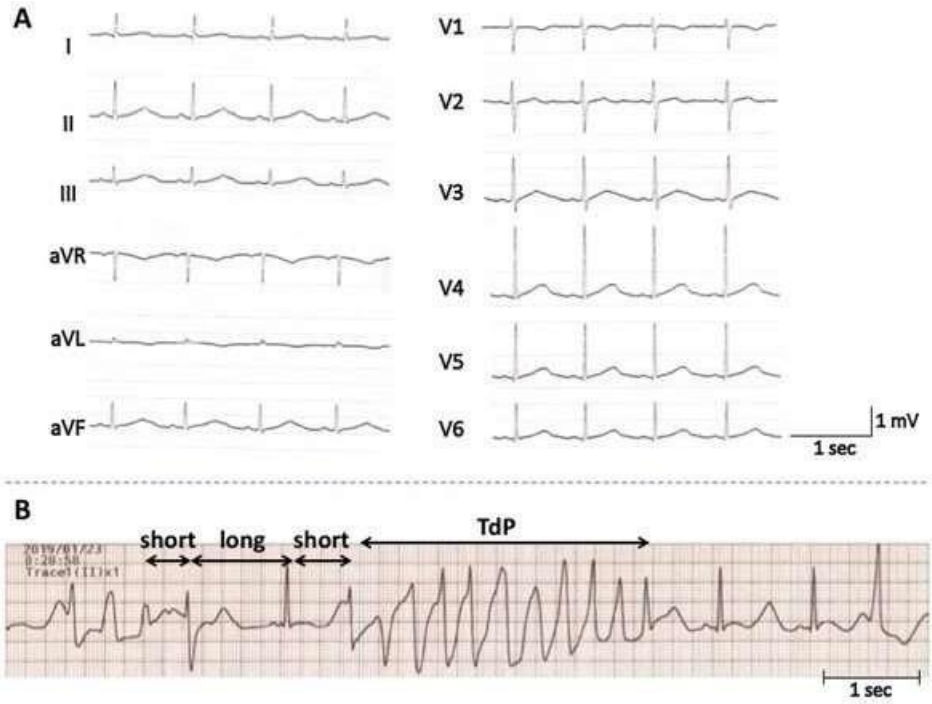

Figure 1.A) Twelve-lead electrocardiogram on admission.**B)** Tracings of bedside continuous single-lead ECG after admission. Torsades de pointes spontaneously occurred with typical initiating the “short-long-short” sequence.

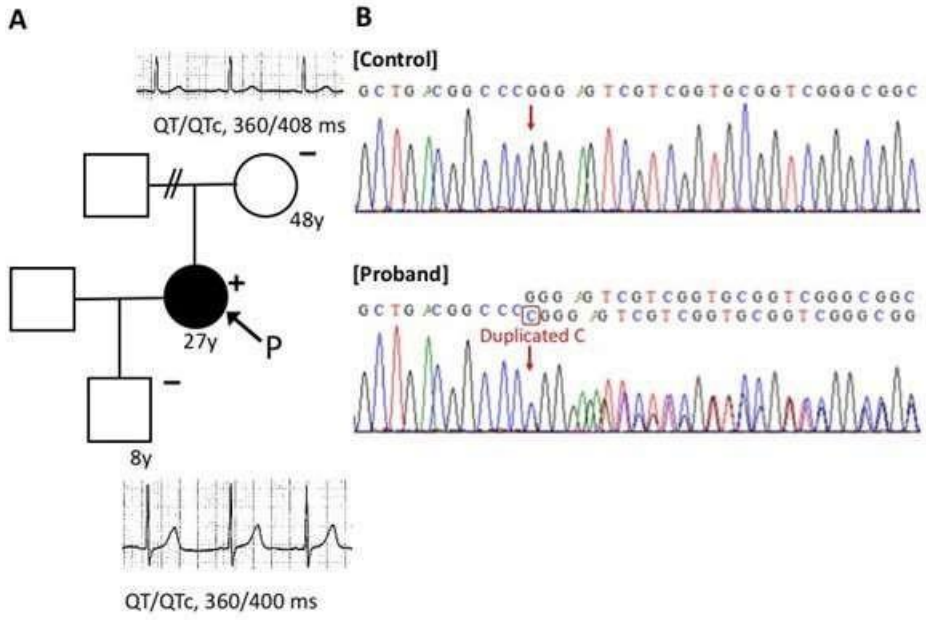

Figure 2. A) Pedigree ofKCNH2, p.R176fsX331. Circles and squares indicate females and males, respectively. Closed symbol indicates a historyof syncope.Plussignsindicatevariantpositivesubjects,whereasminussignsindicatevariantnegativesubjects.Theblackarrowindicatestheprobandof thefamily.ElectrocardiogramsinleadV5ofthepatient'smotherandsonshowednoQTprolongation.**B)**Electropherogramsof*KCNH2*incontroland the *KCNH2* gene variant, p.R176fsX331(c. 526dupC), in the patient.

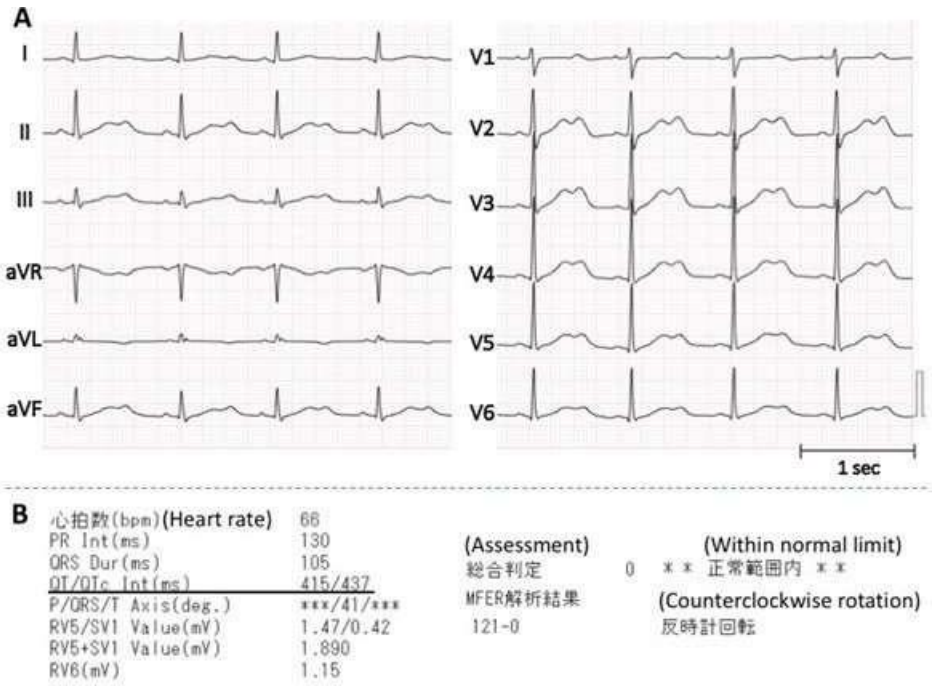

Figure3.A) Twelve-leadelectrocardiogram(ECG)recorded whenthepatientwasaged21 years.**B)**AnautomateddiagnosisbasedonECG.

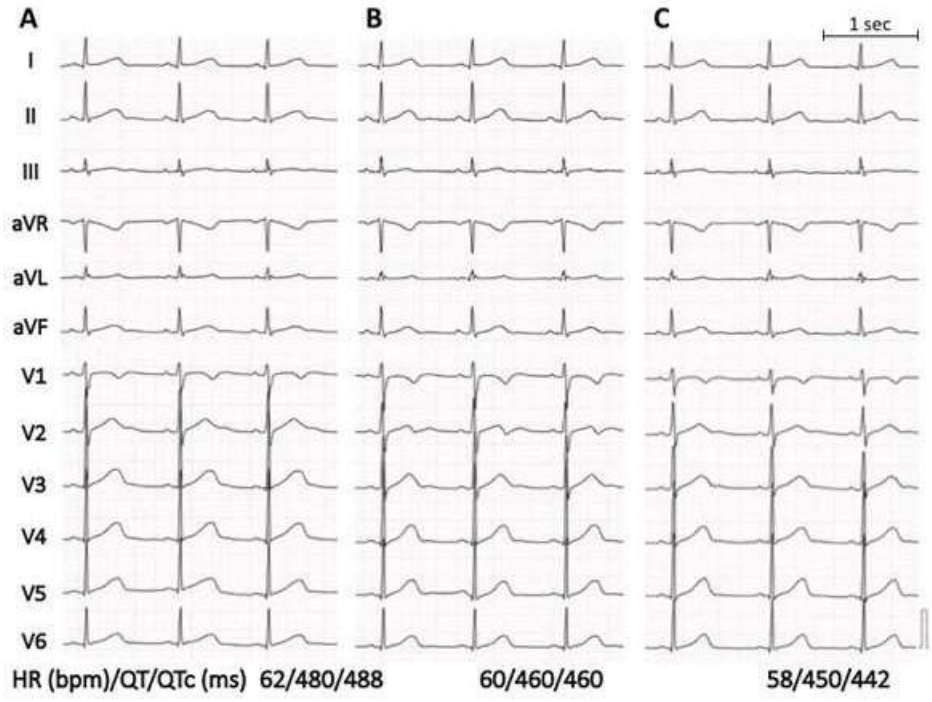

Figure4. Twelve-lead electrocardiograms after daily oral administration of **A)** 5, **B)** 7.5, and **C)** 10 mg carvedilol.

5. Discussion

This report describes a case of recurrent episodes of syncope that persisted 8 years. When initial 12-lead ECG findings were obtained, the physician did not evaluate data carefully. Instead, the physician relied on an automated ECG diagnosis that was obtained using ECG analysis software. After the QT interval in the patient's 12-lead ECG was first misinterpreted via an automated ECG diagnosis, no physicians recommended a repeat ECG examination or reviewed prior findings, despite the recurrence of syncope episodes. Cardiac syncope is the second most common type of syncope [1], and arrhythmias, including TdP, are its most common cause [2,3]. Moreover, patients with cardiac syncope have the highest risk of recurrence and are at increased risk of death from any cause related to syncope [1]. ECG facilitates the diagnosis of cardiac syncope and improves the prognosis of patients. Therefore, to ensure an accurate diagnosis and determine the cause of syncope, multiple ECG examinations and careful analysis of results are crucial [2]. Automated ECG diagnosis benefits physicians because it reduces the effort needed to evaluate ECG findings and allows physicians to immediately use findings in the clinic. The automated ECG diagnoses are widely utilized in medical practices with non-expert physicians and medical staff [4]. However, automated ECG diagnoses are not always correct. In particular, QT prolongation is underestimated or unreported via diagnostic software [5,6], and measurement differences between algorithms in the determination of QT interval are larger in patients with congenital [7,8] and acquired [9] long QT interval than in healthy subjects. A previous study revealed that automated ECG diagnosis concluded that findings were "normal" in 42.1% of patients with a prolonged QTc interval [6]. The phenomenon was observed for algorithms of various manufacturers [10]. From these perspectives, automated ECG diagnosis plus over-reading by physicians offer the accurate diagnosis, and long QT syndrome experts strongly advocate manual measurement [5,11,12]. In the present case, apparent and obvious QT prolongation at 21 years of age (Figure 3A) was missed due to an incorrect automated ECG diagnosis. T waves in leads I, II, III, aVR, aVF, and V2-V6 had prominent notches, and the second component of the T wave should have been included in the analysis of the QT interval [11]. The automated ECG diagnosis did not consider the second component of the notched T wave, and instead regarded the endpoint of the first component of the notched T wave as the endpoint of the QT interval. If the physician had self-evaluated ECG findings, they would have noticed the mark- edly prolonged QT interval and bimodal T waves, even if the QT interval was inaccurately measured. The patient was administered carvedilol, a non-selective β- and α1-blocker, from the age of 27, when she was diagnosed with type 2 long QT syndrome. In a prior report, we showed that carvedilol maybe used to effectively treat type 2 long QT syndrome [14]. It was suggested that α1-adrenergic stimulation acutely reduces Kv 11.1 channel activity via the membrane PIP2 pathway [15]. Acute α1-adrenoceptor-mediated reduction in I_{Kr} at lower heart rate would act additionally to prolong action potential durations and may enhance inward current through Na/Ca exchanger. After the administration of carvedilol, the patient had no episodes of syncope and her QT interval at rest shortened considerably.

6. Conclusions

ECG is an essential method that may be used in the examination of

patients with recurrent syncope. Moreover, all physicians should confirmECG withtheir owneyes ifthere is QT prolongationand not rely exclusively on automated ECG diagnosis.

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